

1.0 AMENDMENT

1.1 IN THE CLAIMS

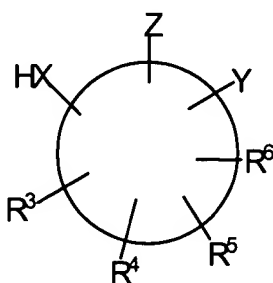
Please cancel claims 32-34 without prejudice and without disclaimer.

Please amend the pending claims as shown below:

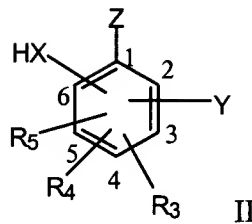
Please add new claims 39-40 as shown below:

1. (Currently Amended) A method of
- a) synthesis of a linear or cyclic peptide,
 - b) synthesis of a C-terminal modified peptide, or
 - c) on-resin cyclization of a peptide molecule, comprising the step of linking a cyclic aromatic or alkyl-auxiliary compound of General Formula II to an primary amine nitrogen atom to form a secondary amine,

[



I]



~~in which the ring optionally comprises one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulphur;~~

~~is of 5 to 7 atoms;~~

~~comprises 3 carbon atoms substituted respectively by XH, Z, and Y; and~~

~~is additionally substituted by groups R^3 and R^4 when the compound is a 5-membered ring,~~

~~or is additionally substituted by groups R^3 , R^4 , and R^5 when the compound is a~~

~~6-membered ring, or is additionally substituted by groups R^3 , R^4 , R^5 and R^6 when the~~

~~compound is a 7-membered ring, in which~~

X is oxygen, ~~sulphur~~sulfur, $\text{CH}_2\text{O}-$, or $\text{CH}_2\text{S}-$;

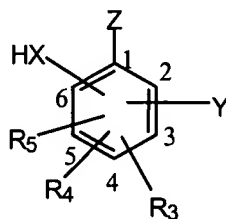
Y is an electron-withdrawing group;

Z is any group which allows the formation of a covalent carbon-nitrogen bond;
and

R^3 , R^4 and R^5 are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, ~~alkoxy~~, aryloxy, XH or Y, or a covalent linkage to a solid support, and

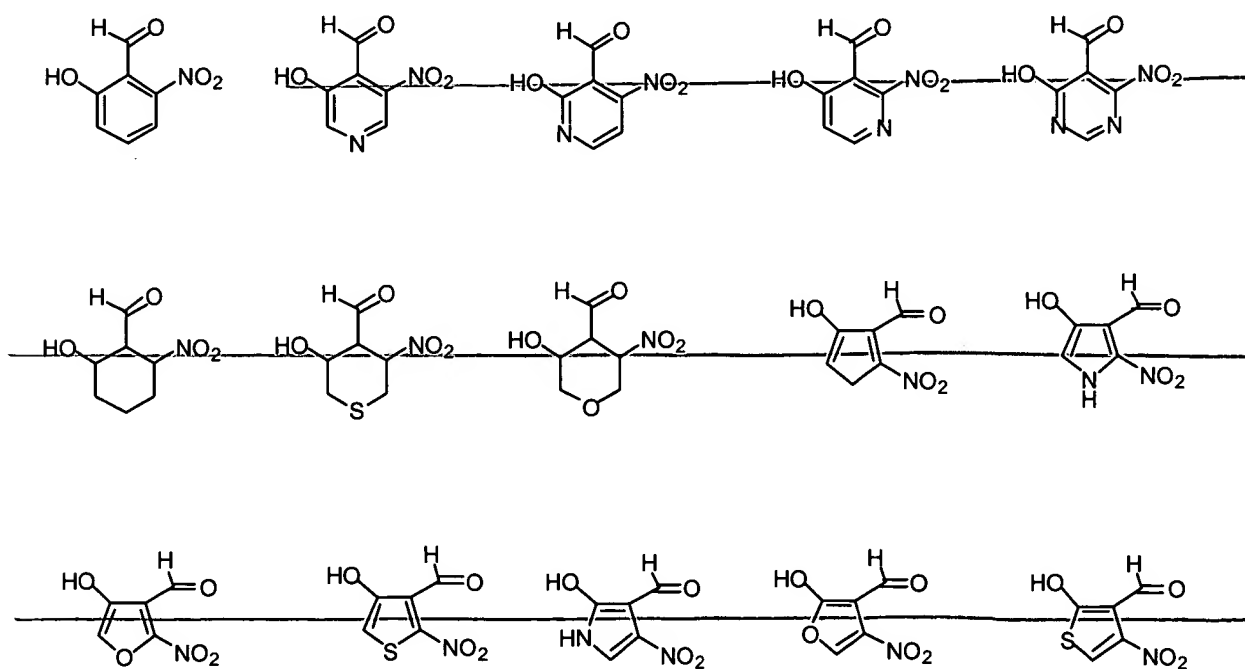
in which R^3 and R^4 , or R^4 and R^5 , ~~or R^5 and R^6~~ can optionally together with the ring form a 5-, 6-, or 7-membered ring, thereby to facilitate conversion of the secondary amine to an amide, and converting the secondary amine to an amide.

2. (Currently Amended) ~~A method according to~~The method of claim 1, in which Y is nitro, ketone, carboxylic ester, amide, nitrile, sulfonamide, sulfoxide, sulfone, sulfonate, fluoride, chloride, bromide or iodide.
3. (Currently Amended) ~~A method according to~~The method of claim 1, in which Z is an aldehyde, alkylalcohol, alkylhalide, or a ketone, or is a halogenated C₁₋₃alkyl group.
4. (Currently Amended) ~~A method according to~~The method of claim 3, in which the halogenated alkyl group is a halogenated methyl group.
5. (Currently Amended) ~~A method according to~~The method of claim 4, in which the halogen is iodine, bromine or chlorine.
6. (Currently Amended) ~~A method according to~~The method of claim 1, in which the auxiliary compound is of general Formula II

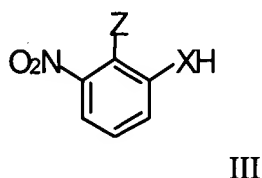


II.

7. (Currently Amended) ~~A method according to~~The method of claim 1, in which the XH group is at position 2 or 3 in ~~General Formula I or General Formula II~~, and Y is at any other position.
8. (Currently Amended) ~~A method according to~~The method of claim 7, in which the XH group is at position 2.
9. (Currently Amended) ~~A method according to~~The method of claim 7, in which Y is at position 6.
10. (Currently Amended) ~~A method according to~~The method of claim 9, in which Y is NO₂.
11. (Currently Amended) ~~A method according to~~The method of claim 1, in which the auxiliary compound is ~~selected from the group consisting of~~

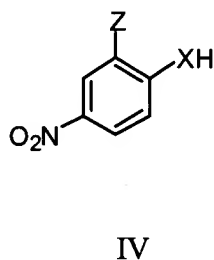


12. (Currently Amended) ~~A method according to~~The method of claim 1 for synthesis of a cyclic peptide, a large peptide, or a difficult peptide, in which the auxiliary compound is of General Formula III



and the auxiliary compound is removed by photolysis following amide bond formation.

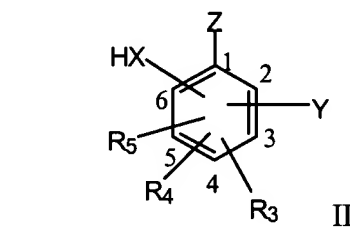
13. (Currently Amended) ~~A method according to~~The method of claim 1 for synthesis of a cyclic peptide, a large peptide, or a difficult peptide containing one or more substituted amide bonds, in which the auxiliary compound is not removed, and the auxiliary compound is of General Formula IV



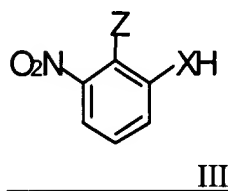
14. (Currently Amended) A method of

- a) synthesis of a compound selected from the group consisting of linear and cyclic peptides, large peptides with a native peptide backbone, and “difficult” peptide sequences,
- b) backbone linkage for the synthesis of peptides, C-terminal modified peptides, or
- c) on-resin cyclisation/cyclization,

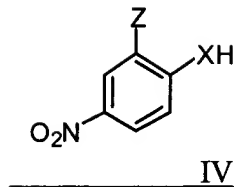
comprising the steps of: linking a cyclic auxiliary compound of ~~General Formula I,~~ General Formula II,



General Formula III,



or General Formula IV



in which X is oxygen, sulfur, CH₂O-, or CH₂S-;

Y is an electron-withdrawing group;

Z is any group which allows the formation of a covalent carbon-nitrogen bond;

and

R³, R⁴ and R⁵ are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, alkoxy, aryloxy, XH or Y, or a covalent linkage to a solid support, and

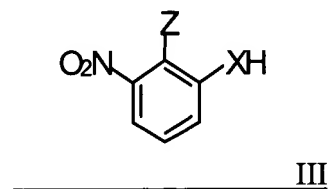
in which R³ and R⁴, or R⁴ and R⁵ can optionally together with the ring form a 5-, 6-, or 7-membered ring

to ~~an~~ a primary amine nitrogen atom to form a secondary amine, thereby to facilitate conversion of the amine to an amide, and converting the secondary amine to an amide.

15. (Currently Amended) ~~A method according to~~ The method of claim 14, in which XH in General Formula III is at position 2, and Y is NO₂ at position 6.

16. (Currently Amended) ~~A method according to~~ The method of claim 1, in which R³, R⁴, and R⁵ and R⁶ are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, and a covalent linkage to a solid support.

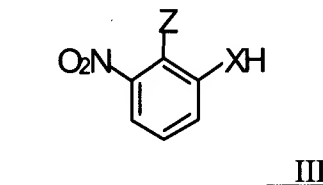
17. (Currently Amended) A method of synthesis of a cyclic peptide, comprising the steps of
- ~~synthesizing~~synthesizing a linear peptide to be ~~eyelised~~cyclized,
 - linking an auxiliary compound as defined in claim 1 to a ~~desired~~ selected primary amine of the linear peptide,
 - activating a ~~desired~~selected carboxylic acid to effect ~~eyelisation~~cyclization, and where necessary inducing ring contraction, and optionally
 - removing the auxiliary compound after complete ~~N-acylation~~N-acylation.
18. (Currently Amended) ~~A method according to~~The method of claim 17, in which ring contraction is induced by heating or by addition of a metal.
19. (Currently Amended) ~~A method according to~~The method of claim 17, in which the auxiliary compound is of General Formula III,



and the auxiliary compound is removed by photolysis.

20. (Currently Amended) ~~A method according to~~The method of claim 17, in which steps a) to d) are performed on a solid support, and are followed by cleavage of the cyclic product from the solid support, ~~and if desired, removal of side chain protecting groups.~~

21. (Currently Amended) ~~A method according to~~ The method of claim 17, in which activation of the C-terminal carboxylic acid is performed in the presence of an auxiliary compound of General Formula III,

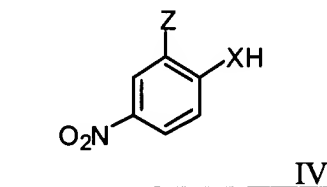


and the ~~eyelisation~~ cyclization is performed by attaching the auxiliary compound to the ~~desired~~ selected amine via the Z-group.

22. (Currently Amended) A method of synthesis of a large peptide with a native peptide backbone, comprising the steps of

- a) ~~synthesis~~ synthesizing a set of peptide fragments to be linked to form a large peptide,
- b) linking an auxiliary compound as defined in claim 1 to the primary amine of the first peptide fragment,
- c) activating the C-terminal carboxylic acid of the second peptide fragment,
- d) adding the second peptide fragment to the first peptide fragment and forming a peptide bond between the two fragments, and optionally
- e) removing the auxiliary compound after N-acylation is complete.

23. (Currently Amended) ~~A method according to~~The method of claim 21, in which the auxiliary compound is of General Formula IV,

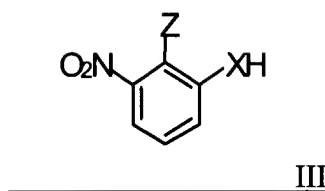


and the auxiliary compound is removed by photolysis.

24. (Currently Amended) A method of synthesis of a difficult peptide sequence, comprising the steps of

- a) linking an auxiliary compound as defined in claim 1 to one or more nitrogen atoms in peptide bonds of a peptide linked to a solid support,
- b) ~~synthesizing~~synthesizing the complete peptide using standard solid phase synthesis methods, and optionally
- c) when synthesis is complete, removing the auxiliary compound.

25. (Currently Amended) ~~A method according to~~The method of claim 24, in which the auxiliary compound is of General Formula III,



and the auxiliary compound is removed by photolysis.

26. (Currently Amended) A method of backbone linkage for synthesis of a linear peptide, comprising the steps of

- a) using an auxiliary compound as defined in claim 1 as a linker linking the α -nitrogen of an amino acid residue in the ~~desired~~selected peptide to a solid support,
- b) assembling the linear peptide using standard solid phase peptide synthesis methods, and optionally
- c) removing the side chain protecting group(s), and/or
- d) cleaving the peptide from the solid support.

27. (Currently Amended) ~~A method according to~~The method of claim 26, in which the ~~carboxylic acid group of the C-terminal amino acid residue of the selected peptide is a modified~~carboxylic acid in which the carboxyl group is replaced by a functional group.

28. (Currently Amended) ~~A method according to~~The method of claim 26, in which the ~~carboxylic acid group of the C-terminal amino acid residue is replaced by~~functional group is an ester, alkylalcohol, acetal or amide group.

29. (Currently Amended) ~~A method according to~~The method of claim 26, in which Y is nitro in position 6, XH is in position 2, and cleavage is performed by photolysis.

30. (Currently Amended) A method of on-resin ~~cyclization~~cyclization of a linear peptide, comprising the steps of

- a) using an auxiliary compound as defined in claim 1 as a linker linking the α -nitrogen of an amino acid residue in the desired peptide to a solid support,
- b) ~~synthesizing~~synthesizing a linear peptide on a solid support, using standard solid phase peptide synthesis methods,
- c) deprotecting the desired amine and carboxylic acid groups,
- d) activating the carboxylic acid group to perform ~~cyclization~~cyclization, and optionally
- e) deprotecting amino acid side chain groups, and/or
- f) cleaving the cyclic peptide from the solid support.

31. (Currently Amended) ~~A method according to~~The method of claim 30, in which Y is a nitro group in position 6, XH is in position 2, and cleavage is performed by photolysis.

32.-34. (Canceled)

35. (Currently Amended) ~~A method according to~~The method of claim 15, in which R^3 , R^4 , and R^5 ~~and~~ R^6 are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, and a covalent linkage to a solid support.

36-38. (Canceled)

39. (New) The method of claim 20, in which side-chain protecting groups are removed after cleavage of the cyclic product from the solid support.

40. (New) The method of claim 22, in which steps (a) to (e) are repeated to add the remaining members of the set of peptide fragments until the large peptide is complete.